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Efficacy of FFP3 respirators for prevention of SARS-CoV-2 infection in healthcare workers

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Nov 16, 2021 • https://doi.org/10.7554/eLife.71131

Version of Record

Accepted for publication after peer review and revision.

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Version of Record published History

December 1, 2021 (This version)

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Abstract

Background:

Respiratory protective equipment recommended in the UK for healthcare workers (HCWs) caring for patients with COVID-19 comprises a fluid-resistant surgical mask (FRSM), except in the context of aerosol generating procedures (AGPs). We previously demonstrated frequent pauci- and asymptomatic severe acute respiratory syndrome coronavirus 2 infection HCWs during the first wave of the COVID-19 pandemic in the UK, using a comprehensive PCR-based HCW screening programme (Rivett et al., 2020; Jones et al., 2020).

Methods:

Here, we use observational data and mathematical modelling to analyse infection rates amongst HCWs working on 'red' (coronavirus disease 2019, COVID-19) and 'green' (non-COVID-19) wards during the second wave of the pandemic, before and after the substitution of filtering face piece 3 (FFP3) respirators for FRSMs.

Results:

Whilst using FRSMs, HCWs working on red wards faced an approximately 31-fold (and at least fivefold) increased risk of direct, ward-based infection. Conversely, after

changing to FFP3 respirators, this risk was significantly reduced (52–100% protection).

Conclusions:

FFP3 respirators may therefore provide more effective protection than FRSMs for HCWs caring for patients with COVID-19, whether or not AGPs are undertaken.

Funding:

Wellcome Trust, Medical Research Council, Addenbrooke's Charitable Trust, NIHR Cambridge Biomedical Research Centre, NHS Blood and Transfusion, UKRI.

Editor's evaluation

Respiratory protective equipment that is recommended in the UK for health-care workers caring for COVID-19 patients comprises a fluid resistant surgical mask (FRSM), and in case of procedures that generate aerosols FFP3 respirators are to be used. In this study, health-care workers using FRSMs, while working on COVID-19 wards faced an approximately 31-fold increased risk of ward-based SARS CoV-2 infection. After changing to FFP3 respirators, this risk was significantly reduced. Thus, FFP3 respirators seem to provide more protection than FRSMs for health-care workers caring for patients with COVID-19.

https://doi.org/10.7554/eLife.71131.sa0

Decision letter | eLife's review process

Introduction

Consistent with World Health Organization (WHO) advice (World Health Organization, 2021), UK Infection Protection Control guidance recommends that healthcare workers (HCWs) caring for patients with coronavirus disease 2019 (COVID-19) should use fluid-

resistant surgical masks (FRSMs) type IIR as respiratory protective equipment (RPE), unless aerosol generating procedures (AGPs) are being undertaken or are likely, when a filtering face piece 3 (FFP3) respirator should be used (UK Government, 2021a). Following a recent update, an FFP3 respirator is now also recommended if 'an unacceptable risk of transmission remains following rigorous application of the hierarchy of control' (UK Government, 2021b). Conversely, guidance from the Centers for Disease Control and Prevention (CDC) recommends that HCWs caring for patients with COVID-19 should use an N95 or higher level respirator (Centers for Disease Control and Prevention, 2019). WHO guidance suggests that a respirator, such as FFP3, may be used for HCWs in the absence of AGPs if availability or cost is not an issue (World Health Organization, 2021).

A recent systematic review undertaken for PHE concluded that: 'patients with SARS-CoV-2 infection who are breathing, talking, or coughing generate both respiratory droplets and aerosols, but FRSM (and where required, eye protection) are considered to provide adequate staff protection' (Public Health England, 2020). Nevertheless, FFP3 respirators are more effective in preventing aerosol transmission than FRSMs, and observational data suggest that they may improve protection for HCWs (Oksanen et al., 2020). It has therefore been suggested that respirators should be considered as a means of affording the best available protection (Ha, 2020), and some organisations have decided to provide FFP3 (or equivalent) respirators to HCWs caring for COVID-19 patients, despite a lack of mandate from local or national guidelines (Buising et al., 2020).

Data from the HCW testing programme at Cambridge University Hospitals NHS Foundation Trust (CUHNFT) during the first wave of the UK severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic indicated a higher incidence of infection amongst HCWs caring for patients with COVID-19, compared with those who did not (Rivett et al., 2020). Subsequent studies have confirmed this observation (Eyre et al., 2020; Cooper et al., 2020). This disparity persisted at CUHNFT in December 2020, despite control measures consistent with PHE guidance and audits indicating good compliance. The CUHNFT infection control committee therefore implemented a change of RPE for staff on 'red' (COVID-19) wards from FRSMs to FFP3 respirators. In this study, we analyse the incidence of SARS-CoV-2 infection in HCWs before and after this transition.

Materials and methods

Study design and participants

Request a detailed protocol

CUHNFT is a tertiary hospital in the UK with approximately 1000 beds. During the pandemic, wards were categorised as 'red', 'amber', or 'green'. Patients with confirmed COVID-19 were cared for on red wards, and patients who had negative SARS-CoV-2 tests and no clinical features of COVID-19 on green wards. Patients awaiting test results, who had clinical features of COVID-19 but a negative test result, or who may have been exposed to SARS-CoV-2 were cared for on amber wards.

The CUHNFT electronic rostering system recorded to which ward(s) individual nurses and healthcare assistants (HCAs) were allocated. Although this does not encompass 100% of ward staff, the data can be used to indicate relative ward size. An average of 42.5 (range 19–72) nurses/HCAs worked on green wards, and 49.6 (range 37–69) worked on red wards. The mean number of beds per green ward was 24.1 (range 5–33) and red 28.1 (range 26–33). The mean number of nurses and HCAs per bed was 0.41 (range 0.24–0.58) on green wards and 0.31 (range 0.24–0.42) on red wards.

A change to RPE for staff on red wards from FRSMs to FFP3 respirators was announced on 22/12/20. FFP3 respirators were assigned to staff following fit testing. HCWs on green wards continued to wear FRSMs. HCWs on all wards also wore eye protection. The following types of FFP3 respirator were used during the study period: 3 M 9330+, 3 M 1863, Easimask FSM18, and Mexin MX2016v. HCWs who did not pass fit testing with the masks available used either a JSP half mask respirator or a powered air purifying respirator (Tornado or Easiair).

A comprehensive PCR-based HCW screening programme is established at CUHNFT, with symptomatic testing offered as required and asymptomatic testing offered to all HCWs weekly (Rivett et al., 2020; Jones et al., 2020). From 22/12/20, twice-weekly swabbing was offered on red wards and on wards where the most vulnerable patients were cared for (e.g. transplant and oncology patients). Cases were identified from a database of all positive results, which additionally encompasses positive results from community testing. This recorded the date of swab, onset of symptoms (if present) and in which clinical area the HCW worked.

The start of the study period was taken to be 02/11/20, coinciding with an increase in community incidence of SARS-CoV-2 infection and formal implementation of weekly asymptomatic screening for all staff members. By default new infections on or prior to 27/12/20 were attributed to exposure before the change in RPE. Infections detected later

than this date were attributed to exposure after the change in RPE. This timing was chosen to reflect the median incubation period of SARS-CoV-2 (5.1 days), with 27/12/20 falling 5 days (inclusive) after the change in RPE (Lauer et al., 2020; McAloon et al., 2020). Since staff testing was not conducted at weekends, eight complete weeks were assessed in total prior to the change in RPE (Table 1).

Table 1

Weekly numbers of cases amongst HCWs on red and green wards, and cases per HCW day weeks following the change in RPE are highlighted in grey.

Community incidence (total cases per week) is shown for the East of England, UK, with raw data shown in Figure 1—source data 1.

Week	Week start	Red cases	Red HCW days	Red cases per 10^3 HCW days	Green cases	Green HCW days	Green cases per 10^3 HCW days	Excluded cases	Total	Community
1	02/11/2020	0	98	0	5	3255	1.54	16	21	7876
2	09/11/2020	2	98	20.41	7	3241	2.16	33	42	9499
3	16/11/2020	1	198	5.05	3	3141	0.96	26	30	7998
4	23/11/2020	1	238	4.20	5	3101	1.61	24	31	7203
5	30/11/2020	3	238	12.61	6	3101	1.93	20	29	9441
6	07/12/2020	5	238	21.01	10	3101	3.22	33	48	16,535
7	14/12/2020	1	238	4.20	7	3101	2.26	41	49	31,219
8	21/12/2020	3	238	12.61	10	3101	3.22	56	69	37,259
9	28/12/2020	2	357	5.60	20	2982	6.71	58	80	50,110
10	04/01/2021	4	505	7.92	34	2834	12.00	70	108	41,663
11	11/01/2021	5	848	5.90	33	2491	13.25	63	102	31,341

HCW, healthcare worker; RPE, respiratory protective equipment.

A programme of SARS-CoV-2 vaccination using the BNT162b2 COVID-19 vaccine commenced at CUHNFT on 08/12/20 (Jones et al., 2021). In line with UK national guidance, the programme initially prioritised local residents over the age of 80.

However, some HCWs who had been identified as at high risk from SARS-CoV-2 infection were also vaccinated, and were additionally prevented from working on red wards. From 08/01/21, the programme switched to vaccinating HCWs, with initial priority being given to staff on red wards. To avoid the potential for confounding, the final week of the study period commenced on 11/01/21, since minimal effect is expected in the first 7 days after the first dose of vaccine (Polack et al., 2020).

Because of the rising number of admissions to CUHNFT with COVID-19, the number of red wards was increased from one at the beginning of November 2020 to seven by the week starting 11/01/21. Six wards therefore changed from green to red during the period of data collection. Of 609 positive results over the entire study period, 169 (27.8%) were included in this study. Exclusions encompassed HCWs who were not ward based or worked between different wards with different red/amber/green status (269/609, 44.2 % of positive results), HCW working on amber wards (9/609, 1.5%), non-clinical staff (141/609, 23.1%), and staff working in critical care areas (21/609, 3.5%), where different RPE was used throughout (Table 1).

If a staff member tested positive within 5 days of their ward changing colour, their case was classified according to the red/green status of their ward 5 days before their positive test (to allow for the incubation period, as above). The effects of changing the interval from 5 days to between 3 and 7 days explored.

General statistical analysis

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The number of 'HCW days' for each week of the study was calculated for each category of ward. Rostering information was used to identify the number of nurses and HCAs regularly assigned to each ward on each of the 7 days of the week. Data describing the number of other staff on each ward was not available, but was assumed to be proportional to the number of rostered HCWs, calculations being performed in terms of nurse and HCA numbers.

Where $w_{X,d}$ denotes the number of HCWs on wards of type X on day d, the weekly numbers of ward days for week i, denoted $W_{X,i}$, were calculated as the sums of these values across that week.

$$W_{X,i} = \sum_{d \in i} w_{X,d}$$

Details of community incidence were calculated from publicly available data describing

the East of England region of the UK (Wellcome Sanger Institute, 2021; https://coronavirus.data.gov.uk/details/cases, data downloaded on 12/06/21), and were calculated as the sum of the number of cases reported in each week of the study. Raw data are shown in Figure 1—source data 1. Correlations between cases per ward day and community incidence were calculated using the Wolfram Mathematica software package, version 12.3.1.0.

Mathematical modelling

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In order to quantify the effect of the change in RPE upon cases in red wards, a mathematical model was developed, considering the numbers of cases observed amongst HCWs as arising from a combination of ward-specific infection risks, which relate directly to working on a red or green ward, and non-ward-specific risks, which include infections arising from the community. We first wrote expressions for the infection risk facing workers in different types of wards on week *i*. For HCWs on green wards we write

$$\lambda_i^G = (kC_{i-1} + g)W_{G,i}$$

Where critical care wards were included in the model we write, similarly:

$$\lambda_i^C = (kC_{i-1} + c)W_{C,i}$$

Cases on red wards were split according to whether they arose prior to the introduction of FFP3 masks (R_1) or after that point (R_2), giving:

$$\lambda_i^{R_1} = (kC_{i-1} + r_1)W_{R_1,i}$$

$$\lambda_i^{R_2} = (kC_{i-1} + r_1)W_{R_2,i}$$

Here, the term k is a constant, whilst the value C_{i-1} describes the number of observed cases in the local community in the previous week. Our use of community data from the previous week reflects a generation time for SARS-CoV-2 of approximately 7 days (Volz et al., 2021); we assumed that HCWs diagnosed with COVID-19 infection during this study would have been infected by individuals who were diagnosed in the previous week. The model parameters g, c, r_1, and r_2 describe ward-specific infection risks. FFP3 masks were used from the 23rd December onwards.

Model parameters were optimised using a likelihood framework, identifying the maximum value of the term; here, the number of cases on each type of ward each week, denoted X_i, was represented as emissions from a Poisson distribution with parameter equal to the total risk of infection.

$$L = \sum_i \left[\sum_X log \frac{\lambda_i^{X_i}}{X_i!} \right]$$

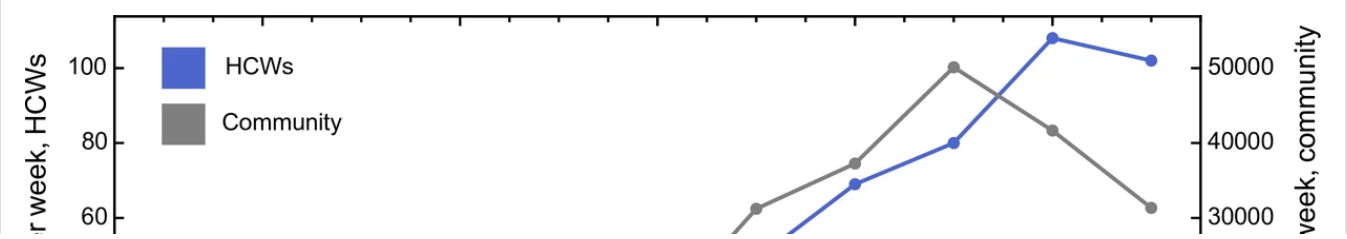
where the sum inside the brackets was calculated over all ward types X.

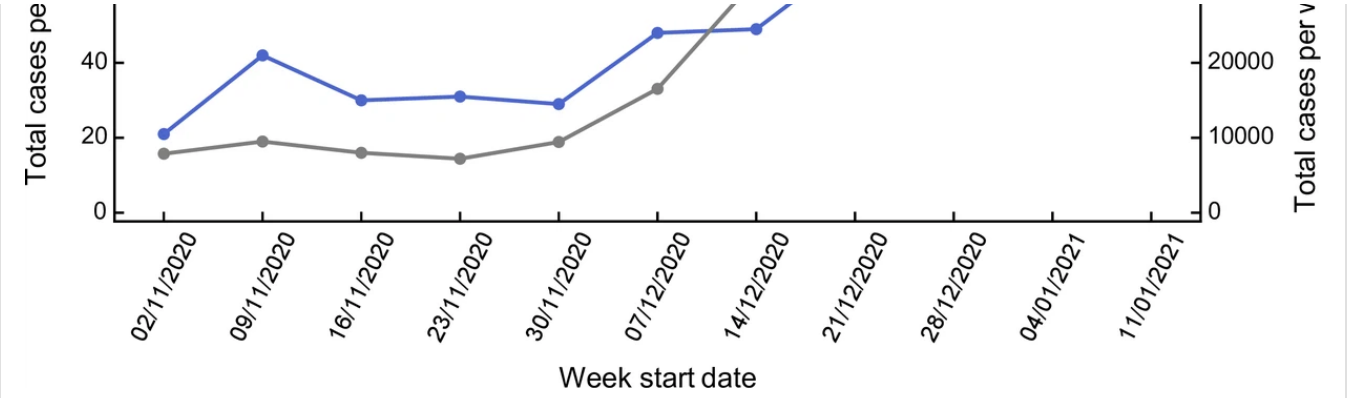
Confidence intervals for each parameter were obtained using this likelihood function. Constrained likelihood optimisations were performed in which the likelihood was optimised subject to a fixed value of the parameter in question. Confidence intervals were defined as the region of parameter space in which the likelihood L was within 2 units of the maximum. Similarly, constrained optimisation was used to identify confidence intervals for parameter ratios such as r_2/r_1.

Results

The total number of cases of SARS-CoV-2 infection amongst HCWs at CUHNFT increased throughout the study period, in keeping with the rising incidence of SARS-CoV-2 in the community (Figure 1 and Figure 1—source data 1). Similar proportions of cases were ascertained by symptomatic testing and asymptomatic screening on both green and red wards, suggesting similar testing-seeking behaviour between staff groups (Figure 1—figure supplement 1). 12.1 % of cases on green wards were amongst allied health professionals, such as physiotherapists and occupational therapists. As expected, there was a significant correlation between community cases and days worked by HCWs on red wards ($p < 0.002$, Pearson correlation test), reflecting increased hospital admissions (Figure 1—figure supplement 2).

Figure 1 with 2 supplements





Comparison between total number of cases amongst healthcare workers (HCWs) and community incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Comparison between total number of cases amongst HCWs and community incidence of SARS-CoV-2. Community incidence is shown for the East of England, UK, derived from https://coronavirus.data.gov.uk/det... see more »

Figure 1—source data 1

Raw case numbers for the East of England region during the period of study.

https://cdn.elifesciences.org/articles/71131/elife-71131-fig1-data1-v2.xlsx

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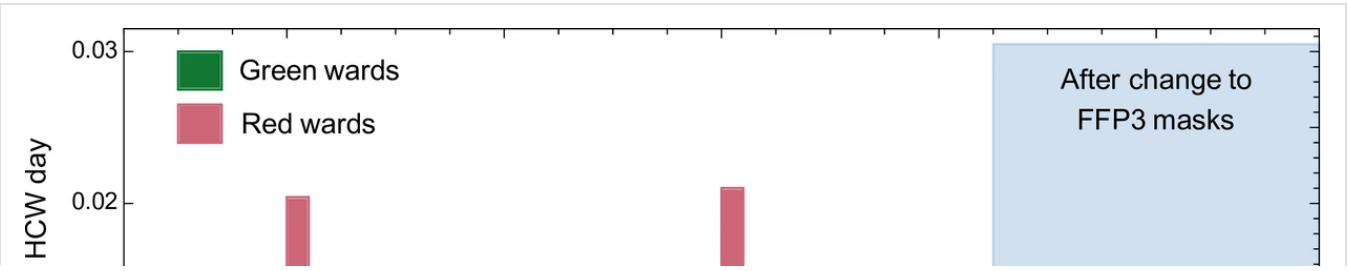
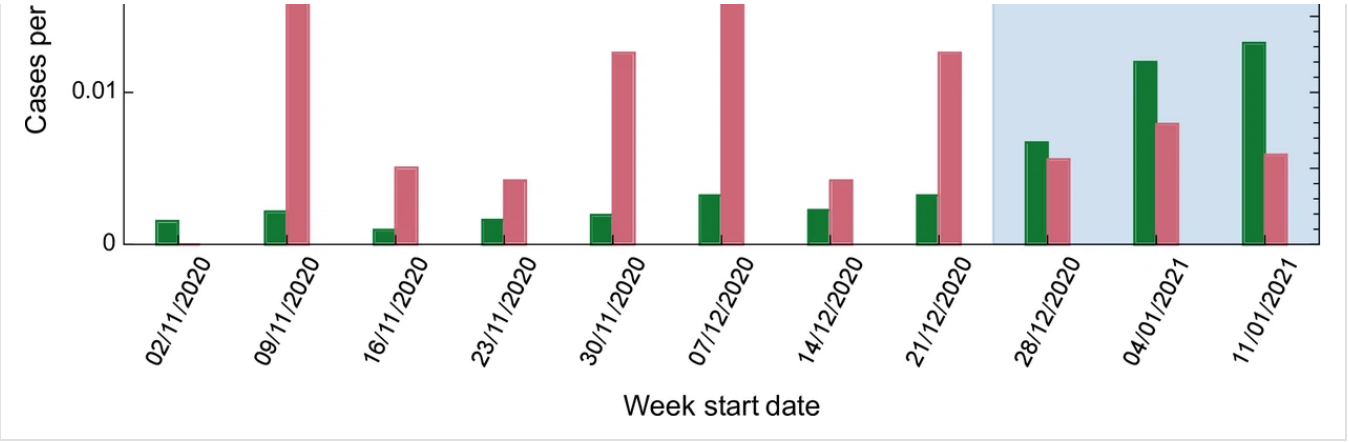
Prior to the change in RPE, cases per HCW day were higher on red compared with green wards in seven out of 8 weeks analysed (p = 0.016, Wilcoxon signed-rank test, Figure 2 and Table 1). Following the change in RPE, the incidence of infection on red and green wards was similar, and not statistically different (p = 0.5, Wilcoxon signed-rank test, Figure 2 and Table 1). Strikingly, there was a strong positive correlation between the incidence of SARS-CoV-2 in the community and the number of cases per HCW day on green (R^2 = 0.80) but not red (R^2 = 0.03) wards (Figure 2—figure supplement 1). Taken together, these results suggest that most cases amongst HCWs on green wards were caused by community-acquired infection, whereas cases amongst HCWs on red wards were driven by direct, ward-based infection from patients with COVID-19.

Figure 2 with 1 supplement

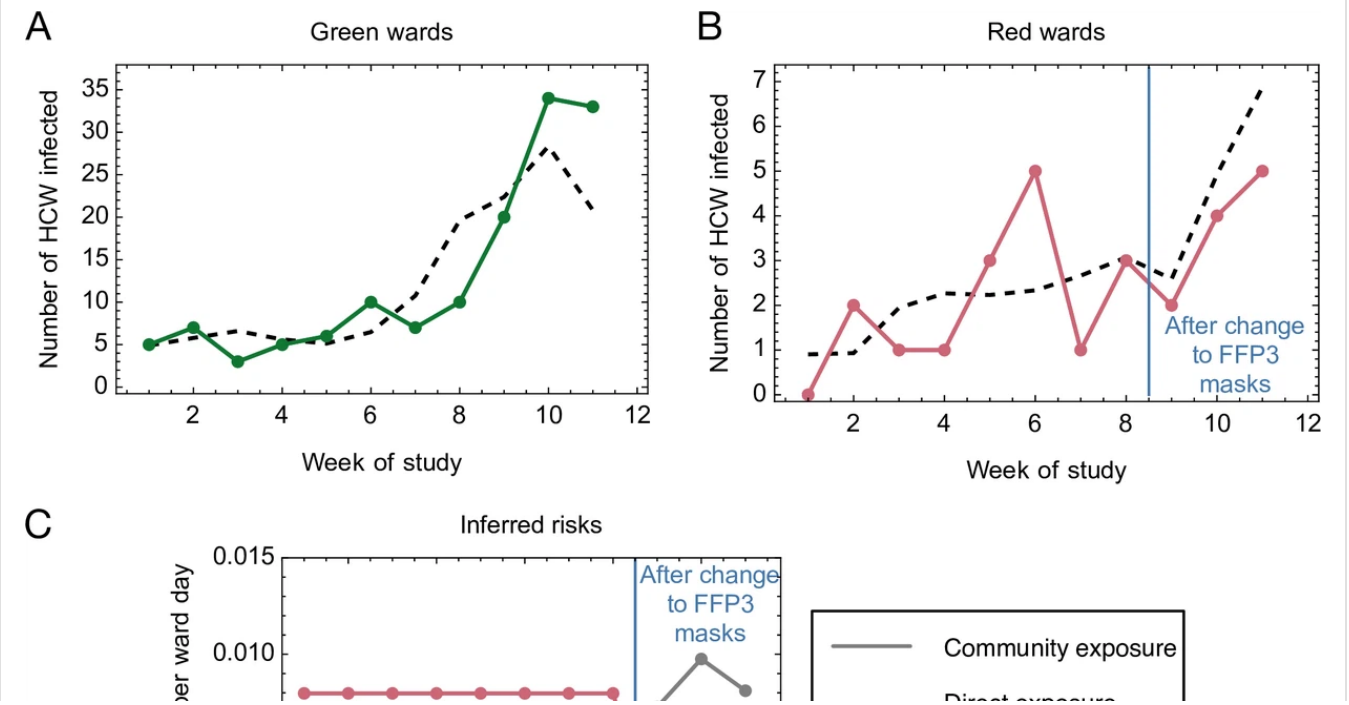


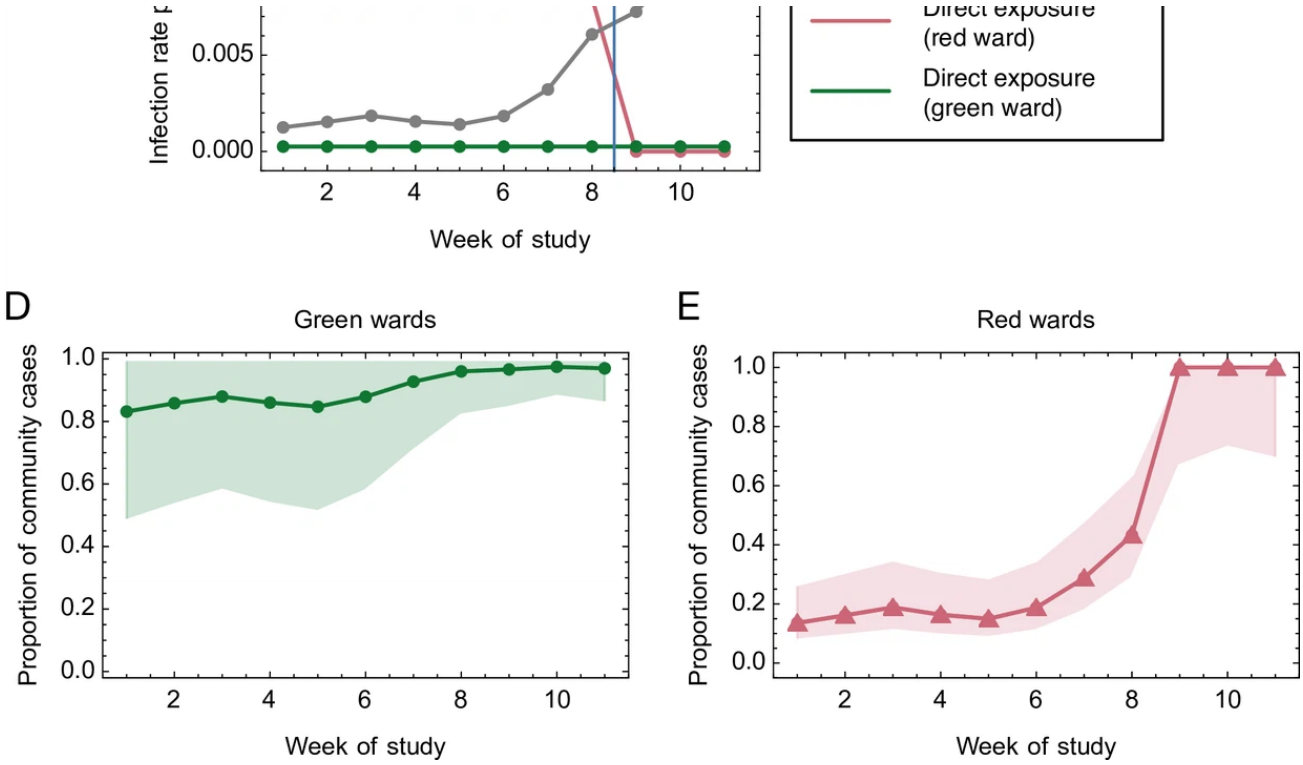


Weekly cases per healthcare worker (HCW) day amongst HCWs on red and green wards prior to and after the change in respiratory protective equipment (RPE).

To further quantify the risk of infection for HCWs working on red and green wards, we generated a simple mathematical model. According to this model, the total risk of infection is divided into a risk from community-based exposure, and a risk from direct, ward-based exposure to patients (ward-specific risk). The risk from direct exposure on red wards was allowed to vary upon the introduction of FFP3 respirators, and was fitted to a maximum likelihood model. Inferred parameters and their confidence intervals are shown in Table 2. Our model produced a qualitatively close fit to the observed numbers of cases (Figure 3A, B).

Figure 3 with 2 supplements





Mathematical modelling of the risks of infection for healthcare workers (HCWs) on red and green wards.

(**A, B**) Comparison of modelled and actual cases. The model (black dashed line) aimed to reproduce the risks of infection amongst HCWs per ward day (**A**) on green wards (green solid line) and (**B**) on red ... see more »

Figure 3—source data 1

Mathematical modelling of the risks of infection for healthcare workers (HCWs) on red and green wards.

https://cdn.elifesciences.org/articles/71131/elife-71131-fig3-data1-v2.xlsx

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Table 2

Statistics and parameter ratios inferred from the model.

Statistic	Model parameter	Maximum likelihood estimate	Confidence interval
Force of community-based infection per community case	k	1.95×10^{-7}	$[1.49 \times 10^{-7}, 2.39 \times 10^{-7}]$
Force of direct infection per HCW day (green ward)	g	2.53×10^{-4}	$[0, 1.10 \times 10^{-3}]$

Statistic	Model parameter	Maximum likelihood estimate	Confidence interval
Force of direct infection per HCW day (red ward, pre-FFP3)	r_1	7.97×10^{-3}	$[3.65 \times 10^{-3}, 1.40 \times 10^{-2}]$
Force of direct infection per ward day (red ward, post-FFP3)	r_2	6.84×10^{-10}	$[0, 3.38 \times 10^{-3}]$
Relative direct risk on red wards post- versus pre-FFP3	r_2/r_1	0.00	[0, 0.478]
Relative direct risk on red ward versus green ward pre-FFP3	r_1/g	31.47	[5.92, ∞)
Relative direct risk on red ward versus green ward post-FFP3	r_2/g	0.00	[0, ∞)

FFP3, filtering face piece 3; HCW, healthcare worker.

The inferred risk of direct infection from working on a green ward was low throughout the study period, and consistently lower than the risk of community-based exposure, which increased in proportion to rising levels of community incidence (Figure 3C). By contrast, the risk of direct infection from working on a red ward before the change in RPE was considerably higher than the risk of community-based exposure, and approximately 31-fold greater than the corresponding risk from working on a green ward (confidence interval [5.93, ∞]). Thus, whilst a high proportion of cases on green wards were likely caused by infection in the community, cases on red wards at the beginning of the study period were attributed mainly to direct, ward-based exposure (Figure 3D, E). Critically, our model further suggests that the introduction of FFP3 respirators led to a reduction of between 52% and 100% (maximum likelihood 100%) in the risk of direct, ward-based COVID-19 infection (Table 2, r_2/r_1).

Where ward designations changed (e.g. from green to red), cases were by default attributed to the type of ward on which each positive-testing HCW worked 5 days prior to reporting symptoms (if symptomatic) or testing positive (if asymptomatic). Altering this cutoff did not alter the maximum likelihood inference for the effect of FFP3 respirators (r_2/r_1, 100%), although the lower bound of the effect size varied between 30% and 72% for cutoffs between 3 and 7 days (Figure 3—figure supplement 1). Data collected from critical care wards, where enhanced PPE was used throughout the period of the study, showed a consistently low rate of HCW infection. Again, incorporating these data into the model did not materially affect the outcome, with the introduction of FFP3 respirators associated with a reduction of between 26% and 100% (most likely

94%) in the risk of direct, ward-based COVID-19 infection at the default cutoff (Figure 3—figure supplement 2).

Discussion

HCWs may be exposed to SARS-CoV-2 from contacts in the community, from contacts with other HCWs, and from contacts with patients. In this study, we developed a mathematical model to evaluate the relative magnitudes of these risks, based on data collected during the second wave of the SARS-CoV-2 pandemic in the UK (November 2020–January 2021).

Whilst using FRSMs, the majority of infections amongst HCWs working on red wards could be attributed to direct exposure to patients with COVID-19. In contrast, as community incidence rose, the majority of infections amongst HCWs working on green wards were attributed by our model to community-based effects. After the change in RPE, cases attributed to ward-based exposure fell significantly, with FFP3 respirators providing an inferred 52–100% (most likely 100%) reduction in the risk of ward-based infection from patients with COVID-19.

In keeping with previous observations (Rivett et al., 2020; Eyre et al., 2020; Cooper et al., 2020), our findings therefore suggest that the use of FRSMs as RPE was insufficient to protect HCWs against infection from patients with COVID-19. Conversely, excess infections amongst HCWs caring for patients with COVID-19 may be prevented by the use of FFP3 respirators, in combination with other PPE and infection control measures.

During the study period, the incidence of SARS-CoV-2 in England increased (Office of National Statistics, 2021), with spread of the more transmissible B.1.1.7 (alpha) variant (Davies et al., 2021). By the ninth week of the study, 79 % of cases in Cambridgeshire were caused by this variant (Wellcome Sanger Institute, 2021). Our observations on the use of FFP3 respirators (weeks 9–11) were therefore made at a time when the B.1.1.7 variant predominated, suggesting that they are robust to any associated increase in SARS-CoV-2 transmissibility in a hospital setting attributable to this variant. Whilst likely also to be applicable to the B.1.617.2 (delta) variant, this was not formally evaluated in our study.

Potential confounders of our observations, should they have differed systematically between HCWs on red and green wards and/or have changed over the course of the

study, include:

1. Rates of natural immunity amongst HCWs on red and green wards; however, the frequency of prior SARS-CoV-2 infections was low within CUHNFT. Overall seropositvity revealed by testing in July and August 2020 was 7.2 % (9.47 % amongst staff from red wards versus 6.16 % amongst all other staff) (Cooper et al., 2020).

2. Rates of vaccination of HCWs on red and green wards; however, the proportion of high-risk HCWs at CUHNFT offered vaccination prior to 08/01/21 was very low, and the study period was ended on 17/01/21 (before any substantial impact of vaccination was expected).

3. Frequency of asymptomatic screening of HCWs on red and green wards; however, the proportions of cases ascertained by symptomatic testing versus asymptomatic screening were similar in both settings. In addition, whilst twice-weekly testing was available for red ward staff from week 8 of the study, this would have tended to increase (rather than decrease) the ascertainment of HCW cases on red wards after the change in RPE in week 9.

4. Compliance with infection control measures by HCWs on red and green wards. It is possible that some of the effect of the change in RPE may have been mediated indirectly, by triggering changes in other behaviours; however, this would still be a positive outcome.

5. Exclusion of infections amongst HCWs who worked on wards from multiple categories (such as, both green and red wards); however, this would have tended to minimise any difference in ward-specific risk of infection.

6. Differences in patterns of HCW behaviour on red and green wards, including mixing between HCWs from different areas. For example, staff working on green wards may have been more likely to leave the ward for lunch than staff working on red wards. Whilst such differences could in theory have contributed to the greater risk of HCW infection on red wards, they are unlikely to have changed systematically with the change in RPE. In addition, if mixing between HCWs from different areas led to an increased rate of infection, it would have tended to minimise any difference in ward-specific risk of infection.

This observational study includes a small number of cases in a single Trust, and there may be alternative explanations for the different patterns of infection observed before and after the change in RPE. Our maximum likelihood inference that FFP3 masks (in

combination with other PPE and infection control measures) provide 100 % protection against ward-based infection should therefore be treated with caution; the large confidence intervals calculated for parameters in our model reflect the limited amount of data available. Nonetheless, our results highlight an urgent need for further studies evaluating the appropriate level of RPE for HCWs caring for patients with COVID-19, as well as other respiratory viruses. In accordance with the precautionary principle, we propose a revision of RPE recommendations until more definitive information is available.

ADD A COMMENT

Data availability

All data generated or analysed during this study are included in the manuscript and supporting files. Source data files have been provided for Figures 1 and 3, and their supplements. Figure 2 source data is included in Table 1 in the main text.

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Decision letter

Jos W Van der Meer
Senior and Reviewing Editor; Radboud University Medical Centre, Netherlands

Sarah Logan
Reviewer; University College Hospital London

Stephanie Evans
Reviewer; Public Health England, United Kingdom

In the interests of transparency, eLife publishes the most substantive revision requests and the accompanying author responses.

Decision letter after peer review:

Thank you for submitting your article "FFP3 respirators protect healthcare workers against infection with SARS-CoV-2" for consideration by *eLife*. Your article has been reviewed by 2 peer reviewers, and the evaluation has been overseen by a Reviewing Editor and Jos van der Meer as the Senior Editor. The following individuals involved in review of your submission have agreed to reveal their identity: Sarah Logan (Reviewer #1); Stephanie Evans (Reviewer #2).

The reviewers have discussed their reviews with one another, and the Reviewing Editor has drafted this to help you prepare a revised submission.

Essential revisions:

1. The authors need to mention more about the differences between red and green wards: In terms of:

Number of patients on the wards (bays and side rooms)

Mean number of pts per nurse

Demographic of the HCW surveyed on each ward- equal numbers of Nurses/ AHP's/

doctors

Vaccine uptake as per below.

Staff rest areas.

2. The authors also need to describe more about the testing seeking behaviour of the two staff groups; access to testing, more frequently accessed by a group of HCW who were aware of the range of symptoms of covid. This could leave to an ascertainment bias in the red ward prior to the change in mask wearing.

3. Vaccine roll out:

Most staff working on COVID wards in December 2020 were the first to access the vaccine, and the roll out in most trusts in the UK was not so coordinated. Thus, we imagine this data will be difficult to get, but without it, more needs to be made of that impact.

4. Given the sophisticated mathematical modelling and statistical analysis, please address the danger of trying to overanalyse the intervention with relatively small numbers.

5. With this in mind it would be nice to see data from critical care ward staff, if they were using FFP3 throughout even though the numbers are small.

6. We would recommend to pay some attention in the discussion to the comments from Andrew Goddard from the RCP bulletin.

7. Although the manuscript states that a similar number of HCWs worked on each ward, it would be helpful to see the results displayed as a proportion of staff on red/green wards that became infected, or to model as individual exposure hours rather than ward status but I understand this might be difficult with the small sample size.

8. It would be helpful for the number of red wards (or total exposure time) and C_i+1 to be plotted to give a visual representation of the correlation.

9. As ward colour in the model is determined exclusively by the presence of infected patients and there is a possibility that one infected HCW on a green ward could lead to an outbreak within the HCW population. While this would not affect the result that changing the type of RPE used reduced the infections per ward day of HCWs on red

wards, ignoring the potential for HCWs to seed outbreaks between ward staff could result in a higher proportion of cases being attributed to the community than actually occurred, and I would consider adding a third component of 'positive result in ward staff' to the model.

10. A sensitivity analysis shifting the 5-day cut off for before/after change in RPE and ward classification would also be a nice addition.

11. As staff working across wards are excluded, it is not clear if the full numbers of staff present on the red/green wards are included in estimations of both the number of cases and number of infectious sources (do the staff, and the non-ward based staff, interact similarly with patients and staff from both red and green wards?).

12. It would be interesting to see the results from the critical care wards that are currently excluded. If these wards used FFP3 respirators throughout, (noting the small numbers) it would be very helpful to see the data for this period in these wards as a (albeit limited) control group.*Reviewer #1:*

Understanding how best to protect healthcare workers from infection at work with SARS- CoV2 is absolutely vital. Much of the interventions to date have been done in an era where the evidence was emerging at the same time as interventions instigated. With that in mind the approach by Cambridge University trust to go above PHE guidance and use FFP3 masks on COVID wards and then for the authors to try to evaluate this impact is absolutely the right approach. There is a clear drop off in infections in healthcare workers on COVID wards in December 2020 after this change was made. There may be several reasons for this not just the prevention of inhalation of aerosols.

The action of donning and doffing an FFP3 mask produces a change in behaviour in the HCW. The need to change one's mask after leaving a clinical area, the discomfort of an FFP3 necessitating shorter wear times than alternative Fluid resistant surgical masks, the prompt to the HCW when changing the mask of hand hygeine may all have contributed to the drop in rate.

The drop-in rate correlates also with vaccine role out. Whilst the authors describe this as not having a major impact in the absence of data on the numbers and date of vaccination of staff on the red and green wards it is impossible to draw this conclusion.

To be fair, the authors themselves tried not to sensationalise their data but I suspect that many infection control teams will have noted the study and (reasonably) will have pressure put on them to act if they have not done so already. Understanding the risks in

double-vaccinated staff, ongoing supply chain issues and the fact that at least 20% of FFP3 mask wearers fail a fit test may mean that applying a simple policy to change all to FFP3 will not be without practical challenges.*Reviewer #2:*

In this paper Ferris et al., attempt to use observational data and mathematical modelling to compare the effect of filtering face piece 3 (FFP3) respirators over fluid resistant surgical masks (FRSM) for reducing infection rates in healthcare workers (HCWs) caring for patients with COVID-19 (working on 'red' wards).

The study uses the median incubation period of 5 days to classify new cases as occurring before/after the change in respiratory protective equipment (RPE), and to categorise wards as red and green. This goes some way towards addressing potential confounding that could be introduced by misclassifying either RPE or wards, although this cannot be completely ruled out. Similarly the study is over a sufficient time period that it is reasonable to assume that the effect of vaccines in the HCW population is negligible. Overall the modelling approach, while simple (with only two components of risk: community and ward), is sensible. The Discussion section of this work is fair and balanced, and the concluding statement that this study is not sufficient to provide conclusive evidence but highlights a need for further study into the appropriate RPE for HCWs caring for patients with COVID-19 is faultless.

As explained by the authors the main limitations of the study hinge upon the small numbers. While the model itself is broadly sensible, the fitting of this to the very limited data on HCW infection is problematic. Slightly different assumptions (e.g. changing the criteria for classifying wards from the median) may provide an alternative (but equally good) fit, but give different conclusions.

A further limitation of the model used here is the association between Ci-1 and determination of ward 'colour': Ci-1 will determine how many green and red wards there are. Likewise, community prevalence will determine the number of COVID +ve admissions which in turn may impact onward transmission within the hospital, therefore Ci-1 is associated too with ward risk.

https://doi.org/10.7554/eLife.71131.sa1

Author response

Essential revisions:

1. The authors need to mention more about the differences between red and green wards: In terms of:

Many thanks for this point. We have added additional information under the subheadings below:

Number of patients on the wards (bays and side rooms)

We have added these details to the Methods section, detailing the mean and ranges for numbers of beds on red and green wards:

“The mean number of beds per green ward was 24.1 (range 5 to 33) and red 28.1 (range 26 to 33).”

Mean number of pts per nurse

This data has been added to the Methods section:

“The mean number of nurses and HCAs per bed were 0.41 (range 0.24 to 0.58) on green wards and 0.31 (range 0.24 to 0.42) on red wards.”

Demographic of the HCW surveyed on each ward- equal numbers of Nurses/ AHP's/ doctors

The table details the job roles of the positive-testing HCWs included in the study. It has been included in the paper as Supplementary file 1.

This data suggests that a higher proportion of cases (85.2% versus 77.9%) fell amongst nurses and healthcare assistants (HCAs) for red compared to green wards, and that there were no allied health professional (AHP) cases on red wards but 17 (12.1%) cases on green wards. This difference is understandable, because AHPs tend to work on multiple wards, there were many more green than red wards, and HCWs who worked on both red and green wards were excluded from the study.

Vaccine uptake as per below.

We have clarified in the paper that the HCW vaccination programme did not commence until 08/01/21. We selected 11/01/21 to be the start of the final week of data analysis to

mitigate against vaccination confounding results. The proportion of high-risk HCWs at CUHNFT offered vaccination prior to 08/01/21 was very low.

Clarification of this is included in two sections of the paper:

Discussion

"(b) Rates of vaccination of HCWs on red and green wards; however, the proportion of high-risk HCWs at CUHNFT offered vaccination prior to 08/01/21 was very low, and the study period was ended on 17/01/21 (before any substantial impact of vaccination was expected)."

Methods

"A programme of SARS-CoV-2 vaccination using the BNT162b2 COVID-19 vaccine commenced at CUHNFT on 08/12/20 [15]. In line with UK national guidance, the programme initially prioritised local residents over the age of 80. However, some HCWs who had been identified as at high risk from SARS-CoV-2 infection were also vaccinated, and were additionally prevented from working on red wards. From 08/01/21 the programme switched to vaccinating HCWs, with initial priority being given to staff on red wards. To avoid the potential for confounding, the final week of the study period commenced on 11/01/21, since minimal effect is expected in the first seven days after the first dose of vaccine [16]."

Staff rest areas.

Similar facilities were available on both red and green wards, and there were no changes in rest areas prior to and after the change in PPE. One caveat is that green ward staff were more likely to leave the ward for lunch than red ward staff, however if an increased rate of infections amongst green ward staff resulted, this would tend to underestimate the difference between both ward types. We have added this to the 'limitations' section of our discussion as follows:

"(f) Differences in patterns of HCW behaviour on red and green wards, including mixing between HCWs from different areas. For example, staff working on green wards may have been more likely to leave the ward for lunch than staff working on red wards. Whilst such differences could in theory have contributed to the greater risk of HCW infection on red wards, they are unlikely to have changed systematically with the change in RPE. In addition, if mixing between HCWs from different areas led to an increased rate of infection, it would have tended to minimise any difference in ward-

specific risk of infection."

2. The authors also need to describe more about the testing seeking behaviour of the two staff groups; access to testing, more frequently accessed by a group of HCW who were aware of the range of symptoms of covid. This could leave to an ascertainment bias in the red ward prior to the change in mask wearing.

Many thanks for this point. Testing seeking behaviour of the two staff groups was very similar. This was evidenced by the similar proportions of cases ascertained by symptomatic testing and asymptomatic screening on both green and red wards (Figure 1—figure supplement 1). We have already highlighted this point in the Results section, however have now clarified this point further, modifying the second sentence of the results to read:

"Similar proportions of cases were ascertained by symptomatic testing and asymptomatic screening on both green and red wards suggesting similar testing-seeking behaviour between staff groups (Figure 1—figure supplement 1)."

Furthermore, access to testing was identical in the initial part of the study, with symptomatic testing offered as required and asymptomatic testing offered to all HCWs weekly. From 22/12/20, twice-weekly swabbing was offered on red wards and on wards where the most vulnerable patients were cared for. We have already stated these points in the Methods section of the paper, however have now added as a limitation:

"Potential confounders of our observations, should they have differed systematically between HCWs on red and green wards and/or have changed over the course of the study, include: …… (c) Frequency of asymptomatic screening of HCWs on red and green wards; however, the proportions of cases ascertained by symptomatic testing versus asymptomatic screening were similar in both settings. In addition, whilst twice-weekly testing was available for red ward staff from week 8 of the study, this would have tended to increase (rather than decrease) the ascertainment of HCW cases on red wards after the change in RPE in week 9."

3. Vaccine roll out:

Most staff working on COVID wards in December 2020 were the first to access the vaccine, and the roll out in most trusts in the UK was not so coordinated. Thus, we imagine this data will be difficult to get, but without it, more needs to be made of that impact.

Many thanks for requesting this clarification. We have already detailed how vaccination was prioritised in the Methods section:

“A programme of SARS-CoV-2 vaccination using the BNT162b2 COVID-19 vaccine commenced at CUHNFT on 08/12/20 [15]. In line with UK national guidance, the programme initially prioritised local residents over the age of 80. However, some HCWs who had been identified as at high risk from SARS-CoV-2 infection were also vaccinated, and were additionally prevented from working on red wards. From 08/01/21 the programme switched to vaccinating HCWs, with initial priority being given to staff on red wards. To avoid the potential for confounding, the end of the study period was therefore taken to be 17/01/21, since minimal effect is expected in the first seven days after the first dose of vaccine [16].”

To clarify this point, we have added details in the discussion about potential confounders of our observations:

“Potential confounders of our observations, should they have differed systematically between HCWs on red and green wards and/or have changed over the course of the study, include: …… (b) Rates of vaccination of HCWs on red and green wards; however, the proportion of high-risk HCWs at CUHNFT offered vaccination prior to 08/01/21 was very low, and the study period was ended on 17/01/21 (before any substantial impact of vaccination was expected).”

4. Given the sophisticated mathematical modelling and statistical analysis, please address the danger of trying to overanalyse the intervention with relatively small numbers.

We do not believe that our mathematical model is particularly complex. In our model HCWs can be infected either via exposure to the virus while they are on a ward (which we describe in terms of a ward-specific infection risk), or they can be infected via exposure to the virus while they are not on a ward (which we describe as a non-ward-specific infection risk). We assume that ward-specific risks are constant within each type of ward, with the exception of a potential change following the change in PPE in red wards, and that non-ward-specific risks are constant across all types of ward. We are not certain that the questions addressed by our study could be evaluated with a less complicated model.

A very valuable point as suggested by the reviewer is that relatively small numbers of cases were available for our study, which additionally considered data from a single hospital and during a specific period of the SARS-CoV-2 pandemic. The size of these

confidence intervals for all of the estimated parameters from our study directly reflects the amount of data we were able to collect. Given more data, we could be more precise in our estimates. We have added a sentence to our Discussion clarifying the extent to which sample size constrains the precision of our estimates.

“Our maximum likelihood inference that FFP3 masks (in combination with other PPE and infection control measures) provide 100% protection against ward-based infection should therefore be treated with caution; the large confidence intervals calculated for parameters in our model reflect the limited amount of data available.”

5. With this in mind it would be nice to see data from critical care ward staff, if they were using FFP3 throughout even though the numbers are small.

We have added data from critical care ward staff to Supplementary File 1. As anticipated by the reviewer, numbers were small. For completeness, we produced an extended version of our model in which critical care wards were included as a separate category to red and green wards (Figure 3 – supplemental figure 2). This did not substantially change the outcome with respect to the effect of introducing FFP3 respirators, which is the central focus of our model.

6. We would recommend to pay some attention in the discussion to the comments from Andrew Goddard from the RCP bulletin.

Very many thanks for this suggestion. We have already communicated with Andrew Goddard about his comments in the RCP bulletin. Of note, Dr. Goddard accepted all of the points we made, stating “I accept all your points”. As the reviewer suggests, some useful additions to the paper can be gleaned from our communications with Dr Goddard, and we note changes to the manuscript that have been introduced below:

– “More regular routine testing of ‘green’ areas appears to have started when the change was introduced.” Staff on green wards were asked to test weekly over the 11 weeks of the study. From 22/12/20 we asked staff on red wards and those green wards with more vulnerable patients (transplant, oncology) to test twice weekly.” This is included in the Methods section: “From 22/12/20, twice-weekly swabbing was offered on red wards and on wards where the most vulnerable patients were cared for (for example, transplant and oncology patients).”

– “The authors state that vaccination didn’t start in the relevant healthcare workers until after the intervention.” We set up our vaccination clinic to start vaccinating staff in early December but were required to vaccinate the over 80s first and so did not start the

staff vaccination programme until 08/01/21. We gave spare vaccines to staff during December and early January from a list of those identified to be vulnerable (who were restricted from working on red wards) and the ED (whose staff were not included in the study). This has been addressed in the Methods section in a paragraph about vaccination, starting “A programme of SARS-CoV-2 vaccination using the BNT162b2 COVID-19 vaccine…”

– “Infection rates in healthcare workers in the second wave were 25% of those seen in the first wave due to previous infection, general improvement in infection control and vaccination.” Our first wave infection rates were possibly lower than some, with positive serology July/August 2020 being 7.2% (9·47% designated Covid-19 areas versus 6·16% in all other staff). Whilst this may have been a confounding factor I think it would have a similar effect on red and green ward staff and so not impact substantially on the findings. However, it is another issue for us to address. We have addressed this point by adding the following to the discussion “Overall seropositvity revealed by testing in July and August 2020 was 7.2% (9·47% amongst staff from red wards versus 6·16% amongst all other staff)”

We have added a further note to our discussion (below), highlighting that the inference of 100% protection from FFP3 respirators should be treated with caution in light of the small numbers in our study. While our study suggests an advantage being gained from FFP3 masks we are keen that they should not be regarded as ‘bullet-proof vests’.

“Our maximum likelihood inference that FFP3 masks (in combination with other PPE and infection control measures) provide 100% protection against ward-based infection should therefore be treated with caution; the large confidence intervals calculated for parameters in our model reflect the limited amount of data available.”

7. Although the manuscript states that a similar number of HCWs worked on each ward, it would be helpful to see the results displayed as a proportion of staff on red/green wards that became infected, or to model as individual exposure hours rather than ward status but I understand this might be difficult with the small sample size.

We have converted the denominator of our statistics to consider representative numbers of HCW days, rather than ward days, based upon rostering information for each of the wards in our study. We do not have readily available information about how many individual HCWs worked on each ward so as to calculate the proportion of staff who became infected. However, the change we have made leads to an estimated risk of infection per HCW day, rather than simply per ward day. Some of the derived numerical values have changed slightly as a consequence of this adjustment, for example the ratio

of red/green risk.

8. It would be helpful for the number of red wards (or total exposure time) and C_i+1 to be plotted to give a visual representation of the correlation.

We thank the reviewer for this suggestion. We found a positive and significant correlation between the number of hours worked on red wards and community incidence, and have shown this in a new Figure 1S2.

9. As ward colour in the model is determined exclusively by the presence of infected patients and there is a possibility that one infected HCW on a green ward could lead to an outbreak within the HCW population. While this would not affect the result that changing the type of RPE used reduced the infections per ward day of HCWs on red wards, ignoring the potential for HCWs to seed outbreaks between ward staff could result in a higher proportion of cases being attributed to the community than actually occurred, and I would consider adding a third component of 'positive result in ward staff' to the model.

This is an important point. The ward colour in the model is determined by the theoretical presence of infected patients, since infected patients can still be present on green wards if undetected as such (Illingworth, Hamilton et al., eLife 2021). Furthermore, the models include the possibility of HCW-to-HCW infection, as they do not distinguish the origin of infections (patients vs HCWs). To address this point, we have added further clarity to the meaning of ‘ward-specific risk’ and ‘non-ward-specific’, or ‘community risk’. HCW-to-HCW infection can occur in two settings: (a) whilst working on the wards. This type of infection would be part of ‘ward-based risk’, and would be susceptible to modification by a change in RPE. This is because throughout the study, FFP3 masks were worn on a sessional basis, being changed at lunchtime and at the end of the day. (b) outside wards. Here, HCWs from both ward settings would experience the same risk of infecting each other, and this would be considered to be part of a ‘community risk’. Of note, one caveat is that HCWs on red wards more frequently ate lunch within the facilities available on the wards, to avoid the need to completely change out of the surgical scrubs worn as part of their PPE. If HCW-to-HCW infections acquired during these lunch breaks accounted for a significant part of the red ‘ward-based risk’, this would tend to act to reduce the effect of the change in RPE. A more nuanced understanding of ‘community’ risks could be gained with more information about patterns of mixing between HCWs during the period of the study, but this information was not available to us.

We have added the following to address these points:

Results:

“To further quantify the risk of infection for HCWs working on red and green wards, we generated a simple mathematical model. According to this model, the total risk of infection is divided into a risk from community-based exposure, and a risk from direct, ward-based exposure to patients *(ward-specific risk)*. The risk from direct exposure on red wards was allowed to vary upon the introduction of FFP3 respirators, and was fitted to a maximum likelihood model.”

Discussion:

“Whilst using FRSMs, the majority of infections among HCWs working on red wards could be attributed to direct exposure to patients with COVID-19. In contrast, as community incidence rose, the majority of infections among HCWs working on green wards were attributed by our model to community-based effects. After the change in RPE, cases attributed to ward-based exposure fell significantly, with FFP3 respirators providing an inferred 52-100% (most likely 100%) reduction in the risk of ward-based infection from patients with COVID-19.”

“Potential confounders of our observations, should they have differed systematically between HCWs on red and green wards and/or have changed over the course of the study, include:

(f) Differences in patterns of HCW behaviour on red and green wards, including mixing between HCWs from different areas. For example, staff working on green wards may have been more likely to leave the ward for lunch than staff working on red wards. Whilst such differences could in theory have contributed to the greater risk of HCW infection on red wards, they are unlikely to have changed systematically with the change in RPE. In addition, if mixing between HCWs from different areas led to an increased rate of infection, it would have tended to minimise any difference in ward-specific risk of infection.”

10. A sensitivity analysis shifting the 5-day cut off for before/after change in RPE and ward classification would also be a nice addition.

We have carried out a sensitivity analysis, shifting the cutoff to values between three and seven days (new Figure 3 —figure supplement 1). Altering the cutoff did not alter the maximum likelihood inference (100%) for the effect of FFP3 respirators, although the lower bound of the effect changed to between 30% and 72% with cutoffs between 3 and 7 days.

11. As staff working across wards are excluded, it is not clear if the full numbers of staff present on the red/green wards are included in estimations of both the number of cases and number of infectious sources (do the staff, and the non-ward based staff, interact similarly with patients and staff from both red and green wards?).

Many thanks for this point. Calculations of staff numbers on red and green wards were performed in terms of the numbers of nurses and health care assistants rostered to each ward on each day, based upon weekday and weekend patterns of working on each ward in the study. This provides a proxy for the total number of HCWs on any given ward. Differences in the interactions between HCWs and patients on red and green wards will contribute to differences in the ward-specific risk. Differences in the interactions between HCWs on red and green wards outside of the ward could not be measured.

We have added the following to address these points:

Methods

“The CUHNFT electronic rostering system recorded to which ward(s) individual nurses and healthcare assistants (HCAs) were allocated. Although this does not encompass 100% of ward staff, the data can be used to indicate relative ward size.”

“The number of ‘HCW days’ for each week of the study was calculated for each category of ward. Rostering information was used to identify the number of nurses and HCAs regularly assigned to each ward on each of the seven days of the week. Data describing the number of other staff on each ward was not available, but was assumed to be proportional to the number of rostered health care workers, calculations being performed in terms of nurse and health care assistant numbers.”

“In order to quantify the effect of the change in RPE upon cases in red wards, a mathematical model was developed, considering the numbers of cases observed among HCWs as arising from a combination of ward-specific infection risks, which relate directly to working on a red or green ward, and non-ward-specific risks, which include infections arising from the community.”

Discussion, ‘limitations’ section:

“Potential confounders of our observations, should they have differed systematically between HCWs on red and green wards and/or have changed over the course of the study, include:

(f) Differences in patterns of HCW behaviour on red and green wards, including mixing between HCWs from different areas. For example, staff working on green wards may have been more likely to leave the ward for lunch than staff working on red wards. Whilst such differences could in theory have contributed to the greater risk of HCW infection on red wards, they are unlikely to have changed systematically with the change in RPE. In addition, if mixing between HCWs from different areas led to an increased rate of infection, it would have tended to minimise any difference in ward-specific risk of infection."

12. It would be interesting to see the results from the critical care wards that are currently excluded. If these wards used FFP3 respirators throughout, (noting the small numbers) it would be very helpful to see the data for this period in these wards as a (albeit limited) control group.

Many thanks for this suggestion; we have now addressed this in point 5 above.

https://doi.org/10.7554/eLife.71131.sa2

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Funding

Wellcome Trust (108070/Z/15/Z)

- Michael P Weekes

Addenbrooke's Charitable Trust, Cambridge University Hospitals

- Michael P Weekes

NIHR Cambridge Biomedical Research Centre

- Michael P Weekes

Medical Research Council (MR/P008801/1)

- Nicholas J Matheson

NHS Blood and Transfusion (WPA15-02)

- Nicholas J Matheson

UK Research and Innovation (MR/V038613/1)

- Christopher JR Illingworth

Medical Research Council (MC_UU_00002/11)

- Christopher J R Illingworth

Medical Research Council (MC_UU_12014)

- Christopher J R Illingworth

The funders had no role in study design, data collection and interpretation, or the decision to submit the work for publication.

Acknowledgements

This research was funded in part by a Wellcome Trust Senior Clinical Research Fellowship [108070/Z/15/Z] and grants from Addenbrooke's Charitable Trust and the NIHR Cambridge Biomedical Research Centre to MPW. NJM was funded by an MRC Clinician Scientist Fellowship [MR/P008801/1] and NHSBT workpackage [WPA15-02]. CJRI was supported by UKRI through the JUNIPER modelling consortium [MR/V038613/1] and by the Medical Research Council [MC_UU_00002/11, MC_UU_12014]. For the purpose of open access, the authors have applied a CC-BY public copyright licence to any author accepted manuscript version arising from this submission. We would like to thank everyone involved in the development and operation of the SARS-CoV-2 testing programme at CUH and the members of staff who have participated. We would also like to thank the Infection Control and Fit Testing teams.

Ethics

Human subjects: This study was conducted as a service evaluation of the CUHNFT staff testing services and PPE policy (CUHNFT clinical project ID3738). As a study of healthcare-associated infections, this investigation is exempt from requiring ethical approval under Section 251 of the NHS Act 2006 (see also the NHS Health Research Authority algorithm, available at http://www.hra-decision-tools.org.uk/research/, which concludes that no formal ethical approval is required).

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Sarah Logan, University College Hospital London
Stephanie Evans, Public Health England, United Kingdom

Publication history

- Received: June 18, 2021
- Accepted: November 7, 2021
- Accepted Manuscript published: November 16, 2021 (version 1)
- Version of Record published: December 1, 2021 (version 2)

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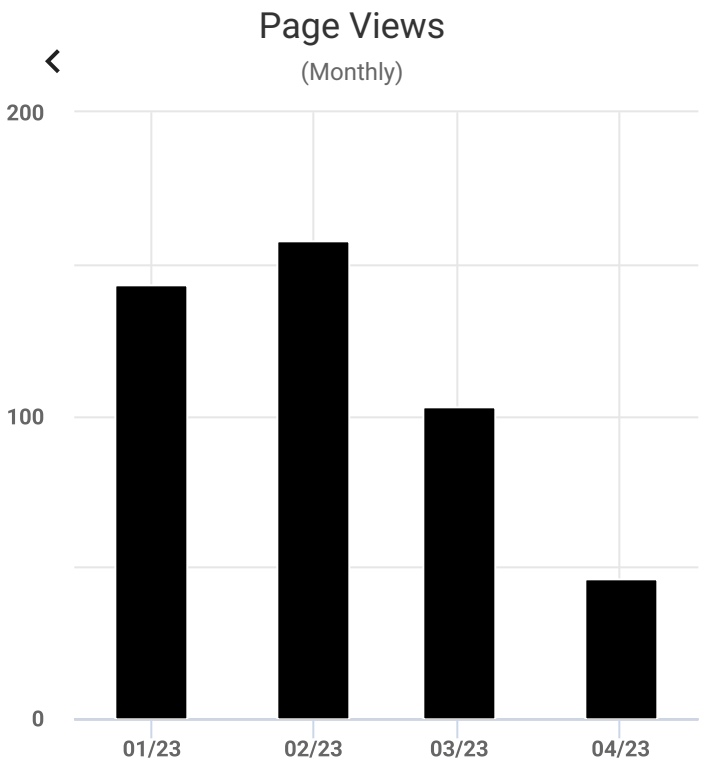

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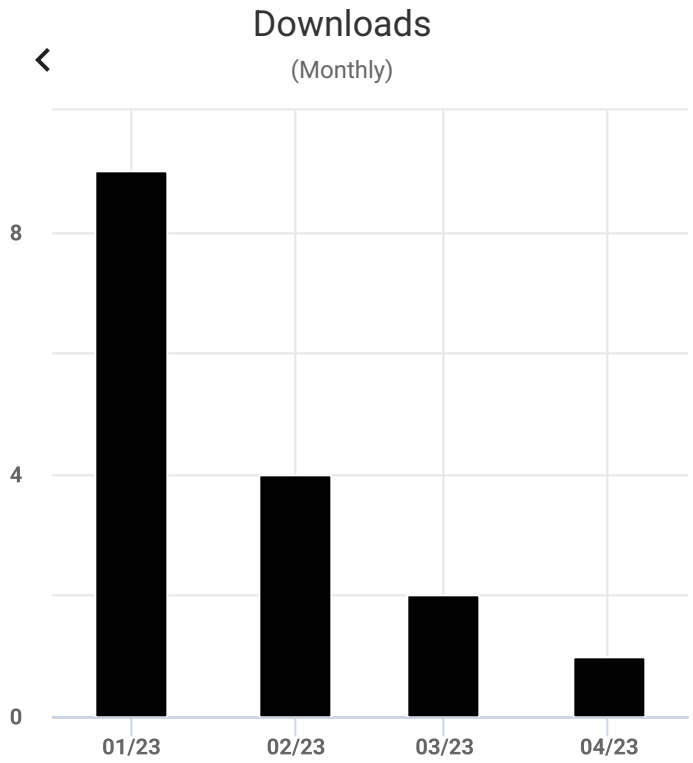

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noted. ISSN: 2050-084X